Author's response to reviews

Title: Subjective health complaints and reduced general function are not associated with tick bites or antibodies to Borrelia burgdorferi sensu lato in blood donors in western Norway

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Author's response to reviews: see over
The editor, BMC Public Health.

Thank you for valuable comments from the referees, a rebuttal of which you find in the following. In the enclosed revised manuscript, changes in responses to reviewer #1 is marked in red, to #2 in green, and to #3 in blue.

COMMENT TO THE EDITOR; NEW REFERENCES ADDED:

Since first submitted, an article has been published that we think should be referred to in this manuscript: Wormser GP, Weitzner E, McKenna D, Nadelman RB, Scavarda C, Molla I, et al. Long-term Assessment of Health-Related Quality of Life in Patients With Culture-Confirmed Early Lyme Disease. Clinical Infectious Diseases. 2015. This, as well as a companion editorial, has been included as references 13 and 14.

REVIEWER #1:

I recommend to use the same expression, Lyme borreliosis instead of interchangeably LB and Lyme disease, throughout the manuscript.

RESPONSE: The term Lyme disease has been replaced by Lyme borreliosis, as recommended (except in the key words, where both expressions are kept). And after explaining the abbreviation LB at the first occurrence, this abbreviation is used throughout.

1. Page 2, line 34: I recommend to replace "tick-borne infections" with "anti borrelial antibodies" because only infection with Lyme borreliae was tested for in this study.

RESPONSE: The sentence has been modified as recommended. («The results do not support any association between tick bites or Borrelia antibodies and subjective health complaints in blood donors in an endemic area for Lyme borreliosis.»)

2. Page 2, line 38: I do not agree that there is much controversy about the clinical manifestations of Lyme borreliosis, but undoubtedly there is much controversy about post-LB symptoms.

RESPONSE: The sentence has been modified accordingly.

3. Page 4, line 75: addition to TESTING serum samples...

RESPONSE: The sentence has been corrected as suggested.

Page 5, line 93: ..., your general function, is today?... Seems like something is missing

RESPONSE: We understand the comment. However, nothing is missing.

Page 7, line 140: Period is missing at the end of sentence.

RESPONSE: Corrected accordingly.

Page 9, line 204: IgG indicates past but also present infection
RESPONSE: The sentence is modified as recommended (".. indicator of former or present infection..")

Page 11, line 249: explain LNB (Lyme neuroborreliosis) when the abbreviation first used.

RESPONSE: Explanation of LNB has been introduced when first occurring, and thereafter "LNB" is used throughout.

Page 13, line 297: I recommend replacing the much broader expression "tick-borne infections" with "anti borrelial antibodies".

RESPONSE: The sentence has been modified as suggested ("The results do not support any association between tick bites or Borrelia antibodies and subjective health complaints in blood donors in an endemic area for Lyme borreliosis.")

Page 19: RF abbreviation should be explained.

RESPONSE: RF (risk factor) is explained in the upper left cell of the table (Table 2).

Page 20: SEM and SHC abbreviations should be explained.

RESPONSE: Explanation of SEM has been introduced in an altered footnote in Table 3 ("Standard error of the mean (SEM) predicted by linear regression with robust variance estimation"). An explanation for SHC has been added in an additional footnote ("SCH: Subjective health complaints. Total SHC score: See text.")
Also, IQR is explained as well ("interquartile range, IQR"), in an additional footnote.

REVIEWER #2:

................. It is unlikely that any of these blood donors did have or did earlier have had disseminated Lyme disease. I think that this very important limitation of the study should also be presented in the conclusion.

RESPONSE: A new sentence has been added to the conclusions section ("A limitation of this study is that very few of the study subjects reported ever having had symptoms indicative of systemic Lyme borreliosis.")

Expect this I only have one more comment: the authors should be consequent in using "Lyme neuroborreliosis" or only "neuroborreliosis" alone throughout the manuscript.

RESPONSE: We have changed all "neuroborreliosis" into "Lyme neuroborrelioses", and the abbreviations "LNB" is used throughout after being explained at first occurrence.

REVIEWER #3:

1. As the unique contribution of this study was to include the SHC questionnaire, the authors should make a greater effort to discuss and explain why the duration of SHC is not included in the data, as the original article of SHC (ref 19: Eriksen et al, 1999) has this included.
RESPONSE: This is a correct observation. We now have included a sentence about these additional questions on duration in the methods section, and in the results section we argue for why we have chosen not to use these data. The reason is the low response rate (mean 60%) to these questions on duration among those reporting any degree of complaint, and using them would be potentially misleading.

2. Furthermore, a discussion is needed whether a dichotomization of SHC into "no complaint" vs any degree of complaint could influence the analysis and results, as the SHC questionnaire definitely discriminates between 0-3. This is all the more interesting also for the discussion part, where several other studies are referred to and discussed, describing "significantly more fatigue..." (ref 31), "more impairment...higher prevalence of ...impairment" (ref 8,9), "more symptoms.." (ref 10), "higher frequency of patients ...frequency of symptoms" (ref 15). A better description of the actual measurement of SHC compared to other measures, and the validation of this, is called for.

RESPONSE: The choice of dichotomizing the SCH responses into “no complaint” vs any degree of complaint was made because there were very few subjects scoring the two most serious responses 2 and 3. The statistical approaches we tried, using the graded responses 0-3 and also when combining the two most serious responses 2 and 3 into one, failed for many questions because the statistical prerequisites for valid analysis were not met because of these low numbers. We have, however, presented the “total SCH score” in the lower half of Table 3, where the severity sum score for all complaints together is presented. We have added a short explanation of this in the methods section (under the subheading “Outcome”, last sentence before “Statistical analysis”). Hopefully the description of the SCH questionnaire now is improved. The questionnaire has shown satisfactory reliability and validity on the Norwegian general population (Ihlebæk C, Eriksen HR, Ursin H. 2004. SHC – et måleinstrument for subjektive helseplager. Tidsskrift for Norsk Psykologiforening, 41(5); 385-387.)

3. The conclusion of the correlation between number of tick bites and good physical fitnes seems to ignore the possible - and more important – correlation mentioned in the discussion part, that people in good health very often have active outdoor activities, exposing them to tick bites. The conclusion on this part is misleading.

RESPONSE: We agree completely with the reviewer on the interpretation of this correlation. We have added a sentence in the conclusions section; “This most probably represents a spurious relationship as both risk factor and outcome are related to a healthy life style.”

4. Same goes for the conclusion on “pseudoneurological” complaints, where none of the individually complaints were sign associated with the risk factors, which is also emphasized in the discussion of the Treib study (ref 31), describing more fatigue etc..

RESPONSE: We have added a sentence in the discussion section; “Also here, a spurious relationship connected to confounding lifestyle factors can be suspected.”, and in the conclusions we have added , “also probably a non-causal relationship”.

Discretionary revisions: The relevance of including a study on Lyme Neuroborreliosis in the discussion could be questioned.
RESPONSE: We have chosen to include the studies on LNB to acknowledge that sequelae to Lyme borreliosis indeed exist, but that such chronic sequelae do not seem to be a problem to the majority of the many tick bitten and/or seropositive individuals in endemic areas.